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TITLE: Restoration of Bladder and Bowel Function Using Electrical Stimulation and Block after Spinal Cord Injury

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
VA Palo Alto Health Care System/PAVIR
3801 Miranda Ave
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of the project is to evaluate the restoration of bladder and bowel function using electrical stimulation and block after spinal cord injury in human subjects.

All staff have been hired and trained, regulatory compliance has been confirmed and maintained from the Institutional Review Board, the Human Research Protection Organization and the Food and Drug Administration.

The medical records of 779 patients with spinal cord injury have been examined to identify potential participants meeting the selection criteria, and participant recruitment and screening is in progress. Implantable stimulators for Stage 1 of the clinical trial have been ordered from the manufacturer.

15. SUBJECT TERMS
Spinal Cord Injuries, Neurogenic Bladder, Electric Stimulation

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1. INTRODUCTION:

This is a prospective Phase 1 clinical trial of an implanted electrical stimulator to improve both continence and voiding in human subjects with chronic spinal cord injury. It will use the existing FDA-approved Vocare stimulator and electrodes, implanting electrodes on the sacral nerves as usual but without performing posterior sacral rhizotomy. Conventional low frequency stimulation will be applied to the sacral nerves at a low amplitude to activate large afferent axons with the aim of inhibiting bladder contraction by neuromodulation, and bladder capacity and continence will be measured. Subjects who show benefit will be offered the implantation of an electrode on each pudendal nerve; these electrodes will be connected to the Vocare stimulator already implanted. The effect of high frequency stimulation of the pudendal nerves through these electrodes to block sphincter contraction and improve electrically stimulated voiding will be measured.

2. KEYWORDS:

Spinal Cord Injuries, Neurogenic Bladder, Electric Stimulation

3. ACCOMPLISHMENTS:

What were the major goals of the project?

1. Confirm and Maintain Regulatory Compliance
2. Coordinate Study Staff for Clinical Trial
3. Participant recruitment, surgery, participant evaluation for Stage 1
4. Surgery, participant evaluation for Stage 2
5. Data analysis and publication

What was accomplished under these goals?

1) Major activities
   - Confirm and maintain regulatory compliance
   - Coordinate study staff for clinical trial
   - Participant recruitment and screening
2) Specific Objectives
   - To improve continence by electrical stimulation in human subjects with SCI
   - To improve voiding by electrical stimulation in human subjects with SCI-planned to commence in year 3
3) Significant results
   - Confirm and maintain regulatory compliance
     - IRB approval initially obtained 9/23/2014 and amended on 1/23/2015 and 7/28/2015 to address DoD requirements
     - HRPO approval – achieved 8/3/2015
   - Coordinate study staff for clinical trial
     - Biomedical Engineer hired 10/15/2014
     - Study Coordinator hired 3/23/2015
     - All staff trained
   - Participant recruitment and screening
     - The medical records of 779 patients with spinal cord injury attending the Spinal Cord Injury Service of the VA Palo Alto Health Care System have been examined to determine which patients potentially meet the inclusion and exclusion criteria of the project. 50 potential participants have been identified. Eight have been provided with information about the study and a copy of the Informed Consent Form, two have signed it, and one has undergone the screening phase to test bladder function with and without electrical stimulation via the surface of the skin. 1st participant consented, screened-achieved 9/30/15
4) Other achievements
   - FDA approval of Investigational Device Exemption for Stage 1 was achieved on 10/10/2015
   - Implantable stimulators for Stage 1 have been ordered from manufacturer

What opportunities for training and professional development has the project provided?

Nothing to report

How were the results disseminated to communities of interest?

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?

1. Further recruitment and screening of participants
2. Implantation of stimulators for Stage 1
3. Evaluation of bladder capacity and continence with implanted stimulator
4. Maintenance of regulatory compliance

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

The use of electrical stimulation to restore both bladder continence and emptying without destructive surgery is likely to make a major difference to the management of the neurogenic bladder and spinal cord injury management.

What was the impact on other disciplines?

Collaboration with biomedical engineers is likely to define new electrical stimulation parameters and protocols for management of the neurogenic bladder.

What was the impact on technology transfer?

The approval by the Food and Drug Administration of Investigational Device Exemption for Phase I of this project will facilitate progress of the project towards technology transfer of the implantable electrical stimulator.

What was the impact on society beyond science and technology?

Nothing to report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to report

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Hiring of Study Coordinator took approximately 5 months during which time the Biomedical Engineer on the project served successfully as acting study coordinator.

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

Not applicable

6. PRODUCTS:

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.
  Journal publications.

Nothing to report

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers, and presentations.

Nothing to report

- **Website(s) or other Internet site(s)**

Nothing to report

- **Technologies or techniques**

Technique being developed for application of high frequency alternating current block

- **Inventions, patent applications, and/or licenses**

Nothing to report

Subset of existing local database documenting bladder function in patients being screened for participation in this project

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: *Graham Creasey*
Project Role: *Project Director*
Nearest person month worked: *4*
Contribution to Project: *Dr. Creasey has worked on interviewing, selecting, recruiting and training of the Study Coordinator, training and coordination of other personnel and on confirming and maintaining regulatory compliance and correspondence with the IRB and HRPO. He has also overseen review of existing databases of patients to identify those potentially meeting selection criteria, met with potential subjects, provided information to allow them to give informed consent, and carried out screening urodynamics.*

Name: *Zoia Latev*
Project Role: *Research Biomedical Engineer*
Nearest person month worked: *4*
Contribution to Project: *Dr.Latev has assisted with interviewing, selecting, recruiting and training of the Study Coordinator, maintaining regulatory compliance and preparing for screening and recruitment. She has also participated in specifying the electrical stimulation equipment required for the project.*

Name: *Shenru Zhao*
Project Role: *Study Coordinator*
Nearest person month worked: *7*
Contribution to project: *Dr. Zhao has maintained regulatory compliance and designed recruitment procedures and created records of potential research subjects, arranged for them to meet with the team and provided them with information required for them to give Informed Consent. She also drafted the application to the Food and Drug Administration for Investigational Device Exemption for Phase I of the project.*

Name: *John Lavelle*
Project Role: *Urologist / Co-Investigator*
Nearest person month worked: *0.5*
Contribution to Project: *Dr. Lavelle contributed to the selection of subjects by review of existing databases of patients, advising on suitability of subjects and screening urodynamics.*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

As planned in the grant application, collaboration has been established with the Functional Electrical Stimulation Center at the VA Medical Center in Cleveland Ohio, which is affiliated with Case Western Reserve University. This Center developed the technique of high frequency alternating current block in animals and has also studied the use of electrical stimulation via electrodes on the surface of the skin for improvement of bladder capacity and continence after spinal cord injury. Both of these techniques will be evaluated in human subjects during this project using implantable electrical stimulators, and the biomedical engineering expertise available from the collaborators at the Functional Electrical Stimulation Center will be crucial in translating their basic research into clinical application in this project.

8. SPECIAL REPORTING REQUIREMENTS

None to Report

9. APPENDICES:

None